EST polypeptide, vectors comprising the nucleic acid molecule, and host cells comprising the vector. The invention further relates to a method of producing a 5'OT-EST wherein the vector comprising the nucleic acid molecules of the invention is used to transform a host cell, and wherein the host cell is then cultured so as to produce the 5'OT-EST polypeptide.

Formal Matters

The Office Action notes that there were discrepancies between the marked and unmarked versions of the claims amended in the previous amendment (filed February 20, 2002). Specifically, the unmarked version of claim 9 recited "or a sequence which *is* at least 90% homologous" while the marked version recited "or a sequence which [are hybridizable under stringent conditions with an oligonucleotide comprising 20 contiguous bases from any one of SEQ ID Nos. 1, 3, 5, 7, 16, or 17; sequences substantially] at least 90% homologous." That is, the word "is" is present in the unmarked, but not the marked version. Applicants submit that the unmarked version was the correct version. However, claim 9 is amended again herein. In order to formally comply with the requirements regarding marked up claims, Applicants provide a marked up version showing changes relative to the claim as pending *before* the February 20, 2002 amendment.

Similarly, the Office Action noted that whereas claim 10 previously recited SEQ ID NO: 31, neither version in the last amendment contained that sequence identifier. Applicants acknowledge that claim 10 was amended to contain the SEQ ID NO: 31 identifier in the amendment filed May 2, 2001. Applicants have herein amended claim 10 to removing the listing of the sequence itself, instead reciting only the SEQ ID NO, and adding further language regarding homology (discussed herein below). The marked-up version shown herein is based on the claim as it occurred after the May 2, 2001 amendment.

Upon review of the file, Applicants note that an IDS was filed on July 14, 2000, but the

initialed Form 1449 has not been received from the Patent Office. Applicants respectfully request that the Examiner acknowledge receipt of the IDS and consideration of the references disclosed therein.

Sequence Compliance

The Office Action objects to the specification because recently amended claims 10, 33 and 34 contain polynucleotide or amino acid sequences without SEQ ID identifiers. As noted above, claim 10 already had the SEQ ID NO: 31 identifier due to the amendment of May 2, 2001. The amendment to claim 10 made in the response filed February 20, 2002 erroneously omitted the sequence identifier from both the marked up and the clean version of the claim. That is, the amendment filed February 20, 2002 was not intended to remove the SEQ ID NO: 31 identifier. Applicants submit that the marked up version of amended claim 10 shown herein reflects the language of the claim as it stood before the February 20, 2002 amendment, marked to show the presently amended form. The SEQ ID NO: 31 identifier is thus present in the claim both before and after the amendments proposed herein. Claims 33 and 34 are amended herein to include SEQ ID NO identifiers. Specifically, the sequence recited in claim 33 is identified by SEQ ID NO: 37, and that in claim 34 is identified by SEQ ID NO: 8. The amendments add no new matter. In view of the amendments, Applicants submit that the application is in compliance with the sequence rules. Applicants therefore respectfully request the withdrawal of the objection.

Specification

The Office Action objects to the specification for the presence of URLs. Applicants have reviewed the specification and amended two occurrences of URLs not addressed in the previous amendment. Specifically, URLs located at pages 12 and 13 have been removed by amendment directed herein above. Applicants submit that the specification is in compliance with the rules and respectfully request the withdrawal of the objection.

The amendment filed February 20, 2002 is objected to for new matter. Specifically, the amendment is objected to because the priority information inserted includes the statement "all of which are incorporated herein in their entirety" relating to the priority documents referred to. Applicants have herein amended the insertion to remove that language. Applicants respectfully request the withdrawal of the objection.

Rejection of Claims 28 and 31-34 Under 35 U.S.C. § 112 First Paragraph

Claims 28 and 31-34 are rejected under 35 U.S.C. §112, first paragraph for lack of written description. The Office Action states that claim 28 is drawn to a 5'OT-EST or a sequence with at least 90% homology to 5'OT-EST, and claims 31-34 encompass a mutant 5'OT-EST. The Office Action acknowledges that the polynucleotide sequences which encode the polypeptide sequences set forth in SEQ ID NOs: 2, 4, 6 and 16 and the polynucleotide sequences set forth in SEQ ID NOs: 1, 3 and 16 meet written description, but states that the "5'OT-EST or equivalents thereof recited and encompassed by the claims do not meet the written description requirement." The Office Action states that the specification fails to describe any 5'OT-EST polynucleotide sequence beside those defined by SEQ ID NOs in the present specification, and that the claimed embodiments of the nucleic acid encompassed by the term "5'OT-EST" and mutant thereof lack written description. Applicants respectfully disagree.

Claim 28 according to the amendment proposed herein recites "at least one detectably labeled nucleic acid probe of 150 nucleotides or less which is capable of hybridizing to a sequence selected from the group consisting of (a) SEQ ID NOs 1, 3 or 5, and (b) a sequence at least 90% identical to the full length of a said sequence as determined by BLAST analysis using default parameters." Applicants submit that the language of the amendment adding reference to BLAST analysis is supported at page 11, lines 29-34. Default parameters are set out in the specification at page 11, line 35 to page 14, line 5. Applicants submit that the recitation of the specific sequences by SEQ ID NO, combined with the teachings provided in the specification

which describe how to determine sequence homology by a specific algorithm (BLAST), using specific alignment parameters (default values), would convey with reasonable clarity to those skilled in the art that, as of the filing date, Applicants were in possession of the claimed invention. Further, one skilled in the art would readily know whether a given nucleic acid sequence falls within the coverage of the claims. In view of the proposed amendment, Applicants respectfully request the withdrawal of the §112, first paragraph written description rejection of claim 28.

Claims 31-34 are rejected for lack of written description because claims 31 and 32 recite "a mutant 5'-OT-EST polypeptide" (claims 33 and 34 do not recite the term, but depend from claim 31 in the alternative). Applicants submit that claims 31 and 32 as proposed to be amended herein do not recite "a mutant 5'-OT-EST polypeptide." Applicants further submit that by amending parent claim 8 as proposed herein, Applicants have set forth more clearly what species of 5'OT-EST polypeptides are encompassed by the parent claims, namely one which is at least 90% homologous to one of SEQ ID NOs 2, 4 or 6 as determined by BLAST analysis using default parameters. Whether a given nucleic acid encoding a 5'OT-EST polypeptide is termed a "mutant" or not is irrelevant with regard to the claim – what matters is that the given nucleic acid encodes a polypeptide that has the structure defined by the claim, i.e., one that is at least 90% homologous to one of SEQ ID NOs 2, 4 or 6 as determined by BLAST analysis using default parameters.

Applicants submit that claim 31 as amended requires that a nucleic acid of claim 8, in vivo, modulates the obesity of an animal which expresses such a 5'OT-EST polypeptide. Again, it is irrelevant whether the nucleic acid or the polypeptide it encodes is termed a "mutant" or not. Its structure and correlated function, i.e., modulation of the obesity of an animal which expresses such a polypeptide, are defined by the terms of the claim as amended. The specification clearly describes the activity of 5'OT-EST sequences in the modulation of obesity, and as discussed

above, parent claim 8 satisfies the written description requirement with respect to the other aspects of claim 31. Applicants therefore submit that claim 31 as amended meets the written description requirement.

Applicants submit that claim 32 as proposed to be amended herein differs in scope from claim 31 in the limitation that the animal is a *transgenic* animal comprising a transgene encoding the 5'OT-EST polypeptide recited in claim 8. Applicants submit that this limitation is clearly described in the specification, and the Office Action does not suggest otherwise. Because, as discussed above, the specification clearly conveys to the skilled artisan that the inventors had possession of the material encompassed by parent claims 8 and 31, as amended, it follows that claim 32, which adds a further well described limitation to the existing claims, also meets the written description requirement.

Finally, with regard to the written description of claims 33 and 34, Applicants assume, because they depend from a claim that recites SEQ ID NOs and because they do not recite the term "mutant," that they were mentioned in the rejection as they depend from claim 31 which did recite a "mutant" 5'OT-EST polypeptide. In view of the proposed amendment of claim 31, applicants submit that this rejection of claims 33 and 34 is moot.

In view of the above, Applicants submit that amended claims 28 and 31-34 meet the written description requirement and respectfully request the withdrawal of the §112, first paragraph rejection of these claims.

Rejection of Claims 8-16, 28 and 31-34 Under 35 U.S.C. § 112 Second Paragraph

Claims 8-16, 28 and 31-34 are rejected under 35 U.S.C. § 112, second paragraph as indefinite.

Claims 8-16, 28, 31 and 32 are rejected for recitation of the phrase "at least 90% homologous." The Office Action states that "depending on the program and/or parameters, the

specification teaches one can obtain different homology results," and concludes that because "the claims encompass the use of parameters which are not specifically defined and are subject to change depending on the method used to determine % homology, therefore the metes and bounds of the claim are not substantively nor clearly defined." Applicants respectfully disagree.

First, Applicants note that claims 31 and 32 do not recite the "at least 90% homologous" phrase, although they ultimately depend from claim 8, which does recite the term. Independent claims 8, 16 and 28 are proposed to be amended herein to recite that the subject nucleic acid is at least 90% homologous to the full length of a given SEQ ID NO "as determined by BLAST analysis using default parameters." The language of the amendment is supported as described herein above. Default parameters are set out in the specification at page 11, line 35 to page 14, line 5. Because claims 8, 16 and 28 as amended set out a specific algorithm and alignment parameters to be applied over the full length of the recited sequence, Applicants submit that the metes and bounds of what is meant by "at least 90% homologous" are definite. It follows that the metes and bounds of claims that depend from independent claims 8, 16 and 28 are also definite with respect to the phrase "at least 90% homologous." Applicants respectfully request the withdrawal of this §112, second paragraph rejection of claims 8-16 and 28 as amended.

Claim 32 is rejected as indefinite because the recitation of "said animal" and "said mutant" lack antecedent basis in claim 30 or independent claim 8. Applicants herein propose the amendment of the claim to depend from claim 31, rather than claim 30. The Office Action stated that such amendment would obviate this rejection.

The Office Action also states, with regard to claim 32, that the claim is "unclear because the limitation for an inherent effect of a particular mutant 5'OT-EST in a transgenic animal does not seem to further limit the nature of the polynucleotide of claims 30 or 8 (or claim 31)." The Office Action states that "it is unclear if certain mutant 5'OT-ESTs in vivo contribute to the obesity and when in the context of a transgenic animal do not contribute a particular phenotype,

or if all mutant forms would contribute to a particular phenotype in vivo." The Office Action further states that "it is unclear how the claim further limits the claims upon which it depends because the polynucleotide always has the same inherent property independent of its intended context use." Applicants respectfully disagree.

First, Applicants note that claims 31 and 32 as proposed to be amended herein do not recite a "mutant." Rather, the nucleic acid sequences encompassed by claims 31 and 32 are those encompassed by parent claim 8 as proposed to be amended herein (which recites sequences which are at least 90% homologous to one of SEQ ID NOs 2, 4 or 6 as determined by BLAST analysis using default parameters), with the added limitations that the 5'OT-EST polypeptide encoded modulates, *in vivo*, the obesity of an animal (claim 31) or a transgenic animal (claim 32) that expresses that polypeptide.

Second, with regard to the so-called "limitation for an inherent effect" of a particular 5'OT-EST, Applicants submit that the limitations recited by claims 31 and 32, namely 1) that the encoded 5'OT-EST polypeptide modulates the obesity of an animal which expresses that 5'OT-EST polypeptide (as required by claim 31), and 2) that the animal which expresses the 5'OT-EST sequence is a transgenic animal (as required by claim 32), provide additional functional limitations over the nucleic acid of claim 8. Specifically, the 5'OT-EST of claim 31 must modulate the obesity of an animal that expresses it, and the 5'OT-EST of claim 32 must be expressed in a transgenic animal. That is, dependent claims 31 and 32 further limit the nucleic acid of claim 8 by affirmatively setting out functional requirements for the claimed nucleic acid.

The Office Action states that it is unclear if certain mutant 5'OT-ESTs in vivo contribute to the obesity and when in the context of a transgenic animal do not contribute to a particular phenotype, or if all mutant forms would contribute to a particular phenotype in vivo. Applicants submit that claim 31 as amended makes it clear that a claimed nucleic acid modulates the obesity phenotype of an animal in which it is expressed. Claim 32 further limits this function required

by claim 31 (modulating obesity phenotype in an animal) by requiring that the modulation occur in a transgenic animal. As such, there is no question of differing function in different animal contexts, but claim 32 specifically reaches the obesity modulating function of the claimed nucleic acid when the animal of claim 31 is a transgenic animal. Applicants respectfully request the withdrawal of the §112, second paragraph rejectionof claims 31 and 32 on these grounds.

Claims 33 and 34 are rejected under §112, second paragraph for recitation of dependence on claim 31. The Office Action states that the specification teaches the specific sequences set forth in the claim are not mutant sequences and it is unclear if claims 33 and 34 encompass mutant sequences which comprise the recited sequences or if these sequences are representative of mutant sequences themselves. Applicants submit that whereas the proposed amendment of claim 31 removes the term "mutant," this rejection of claims 33 and 34 is moot. Applicants have, however, herein proposed to amend claims 33 and 34 to remove dependency from claim 29, which was cancelled in the previous amendment.

Rejection of Claims 8-16, 28 Under 35 U.S.C. § 102(b)

Claims 8-12, 15, 16, and 28 are rejected under 35 U.S.C. § 102 (b) as being anticipated by GenBank sequence entries AA955566, AA421393, AA505752, AA421310, AA2422211, AA24389, AA104180, AA850004, H31115, and H31114. The Office Action states that "the claims recite 90% homologous, not identity and that the specification does not support the equivalence of the terms homology and identity." The Office Action continues that " '90% homologous' could reasonably be interpreted to encompass % homology of a given sequence for local similarity comprising any of the specific sequences recited in the instant claims," and concludes that because specification teaches that the ESTs cited each encode a polypeptide which shares homology to the instantly claimed 5'OT-EST, the cited ESTs anticipate the claims. Applicants respectfully disagree.

Applicants submit that claim 8 as proposed to be amended herein is not anticipated by the cited ESTs because none of the cited ESTs, which are all 582 nucleotides in length or shorter, can encode a polypeptide that is "at least 90% homologous, as determined by BLAST analysis using default parameters to the full length of the sequence set forth in any one of SEQ ID Nos. 2, 4, or 6," as required by the claim as amended. Applicants submit that the shortest amino acid sequence of SEQ ID Nos. 2, 4, or 6 is 200 amino acids long (SEQ ID Nos. 2 and 6). Thus, for a prior art sequence to be at least 90% homologous over the full length of such sequence, to one or more of these recited SEQ ID Nos., the prior art amino acid sequence must be at least 180 amino acids long. Of the GenBank sequences cited above, the longest sequence is 582 nucleotides in length (AA245389), which could maximally encode a 194 amino acid sequence. However, as discussed in the previous response, Applicants have translated this nucleotide sequence using the translate tool available at http://www.expasy.ch/tools/dna.html. The translation returned the following possible reading frames:

5'3' Frame 1

N S D P T S G G E C R A W S D **Stop** G C S G N G **Stop** A I L L G C T N S Y P S T Q T L G
K H C A Y L G P Q K S L C S V P D H L P F F G D G P V V T L R R V Q R F F Y P C L Q V
L P S D E V F C L L L Q L E H F L L F Q L H P S L L L L S P L A L G L S L L H L L G L C F
Q L Q P R Y P **Stop** L L H S P V L V P V P G H Q L P V L R E W L L R L A T A R T P A W
A S C N F L S H V N V N S S L R A R

5'3' Frame 2

I R I Q R Q V V S A E P G V T E V A L E T A E P S S W D V P I P I P V H R P **Stop** A S T V
L I W A P R S L C A Q F L T T C P S L V T A Q L **Stop** L F G E S N A S S I R A S R F S R V
Met K F F A S S C S L S T S C S F S C T Q A C S S **Stop** A L W R W A S A F C T S W A C
A S S C N L A I R S S C I R R F S S R F Q A I S S R C S V N G C C A L L R P E P R L G P R
A I S F R T S T **Stop** T L A **Stop** E R A

5'3' Frame 3

F G S N V R W **Stop** V P S L E **Stop** L R L L W K R L S H P P G **Met** Y Q F L S Q Y T D P R
Q A L C L F G P P E V S V L S S **Stop** P P A L L W **Stop** R P S C N S S E S P T L L L S V P P

G S P E **Stop Stop** S F L P P P A A **Stop** A L L A L S V A P K P A P P E P S G A G P Q P S A
P P G P V L P A A T S L S V A P A F A G S R P G S R P S A P G A P **Stop Met** A A A P C Y
G Q N P G L G L V Q F P F A R Q R E L **Stop** P E S A

3'5' Frame 1

C A L S G **Stop** S S R **Stop** R A K G N C T R P K P G F W P **Stop** Q G A A A I H G A P G A
D G L E P G R E P A N A G A T D S E V A A G S T G P G G A E G **Stop** G P A P E G S G G
A G L G A T E R A R S A Q A A G G G K K L H H S G E P G G T D R R S V G L S E E L Q
L G R H Q R R A G G Q E L S T E T S G G P N K H S A C L G S V Y W D R N W Y I P G G
W L S R F Q S N L S H S R L G T H H L T L D P N

3'5' Frame 2
A R S Q A R V H V D V R K E I A R G P S R G S G R S K A Q Q P F T E H R E L **Met** A W
N R D E N R R **Met** Q E L R I A R L Q L E A Q A Q E V Q K A E A Q R Q R A Q E E Q A W
V Q L K E Q E V L K L Q E E A K N F I T R E N L E A R I E E A L D S P K S Y N W A V T
K E G Q V V R N **Stop** A Q R L L G A Q I S T V L A **Stop** G L C T G I G I G T S Q E D G S
A V S R A T S V T P G S A L T T **Stop** R W I R I

3'5' Frame 3

R A L R L E F T L T C E R K L H E A Q A G V L A V A R R S S H S R S T G S **Stop** W P G
T G T R T G E C R S Y G **Stop** R G C S W K H R P R R C R R L R P S A R G L R R S R L G
C N **Stop** K S K K C S S C R R R Q K T S S L G R T W R H G **Stop** K K R W T L R R V T T
G P S P K K G R W S G T E H R D F W G P K **Stop** A Q C L P R V C V L G **Stop** E L V H P
R R **Met** A Q P F P E Q P Q S L Q A R H S P P D V G S E

As can be seen, the longest amino acid sequence which could be encoded by this nucleotide sequence, when taking into account the presence of stop codons, is 112 amino acids in length, and thus cannot comprise a sequence which is at least 90% homologous to any one of SEQ ID Nos. 2, 4, or 6. The next longest GenBank sequence is 521 nucleotides long, which can maximally encode a 170 residue amino acid sequence, and thus cannot comprise a sequence which is at least 90% homologous as determined by BLAST analysis using default parameters to the full length of any one of SEQ ID Nos. 2, 4, or 6.

Applicants therefore submit that none of the GenBank sequences cited by the Examiner

can encode an amino acid sequence which comprises a sequence which is at least 90% homologous as determined by BLAST analysis over the full length of the sequences recited in the claims as amended. Accordingly, Applicants request that the rejection of claim 8 and its dependents 9-12, 15, 16, and 30-32 be reconsidered and withdrawn.

Claim 28 is said by the Office Action to encompass any probe capable of hybridizing to a 5'OT-EST. The Office Action states that "what is encompassed by '90% homologous' is not clearly defined, and could reasonably be interpreted to encompass % homology of a given sequence for local similarity comprising any of the sequences recited in the instant claims." The Office Action states that "the specification teaches that the ESTs [EST identifiers omitted] each encode a polypeptide which shares homology to the instantly claimed 5'OT-EST," concluding that the cited ESTs anticipate the claims. Applicants respectfully disagree.

Applicants submit that claim 28 as proposed to be amended is drawn to a diagnostic reagent for the detection of mutations, polymorphisms or other changes in 5'OT-EST which may predispose an individual to obesity, comprising at least one detectably labeled nucleic acid probe of 150 nucleotides or less which is capable of hybridizing to a sequence selected from the group consisting of (a) any one of SEQ ID NOs 1, 3 or 6, and (b) a sequence at least 90% identical to the full length of a said sequence as determined by BLAST analysis using default parameters. Applicants submit that all of the EST sequences cited in the Office Action are more than 150 nucleotides in length, and, as such, would not, if used as probes, fall within the size limitation set out in the claim as amended. Support for the size limitation is found in the specification at page 15, lines 30-32. Because the ESTs cited in the Office Action are all greater in length than the 150 nucleotides recited in the claim as amended, Applicants submit that claim 28 is not anticipated by any of the cited ESTs. Applicants respectfully request the withdrawal of the §102(b) rejection as it applies to claim 28.

Applicants propose herein the addition of new claim 35, which is drawn to a method for

the detection of mutations, polymorphisms or other changes in 5'OT-EST which may predispose an individual to obesity, the method comprising hybridizing a nucleic acid sample from an individual to a detectably labeled probe that is capable of hybridizing to a sequence selected from the group consisting of (a) any one of SEQ ID NOs 1, 3 or 5, and (b) a sequence at least 90% identical over the full length of one of SEQ ID NOs 1, 3 or 5, wherein a mutation, polymorphism or other change in 5'OT-EST sequence in the individual is detected. Applicants submit that the ESTs cited in the Office Action do not anticipate this new claim because the cited sequences are not used in a method for the detection of mutations, polymorphisms or other changes in 5'OT-EST which may predispose an individual to obesity. The new claim is fully supported in the specification and adds no new matter.

CONCLUSION

In view of the above, Applicants submit that all issues raised in the Office Action have been addressed herein. Applicants respectfully request reconsideration of the claims. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

Date: 11/22/00

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Marked-up Version of Amendments:

In the Specification

On page 1, replace the paragraph after "Cross Reference to Related Applications" with the following amended replacement paragraph:

This application claims priority under 35 U.S.C. §120 to International Application serial number PCT/GB99/02658, filed August 12, 1999, which claims priority to application serial number GB9910522.3, filed May 6, 1999, and GB9817566.4, filed August 12, 1998 [, all of which are incorporated herein in their entirety].

On page 13, replace the paragraph at lines 20-28 with the following replacement paragraph:

FILTER Mask off segments of the query sequence that have low compositional complexity, as determined by the SEG program of Wootton & Federhen (1993) Computers and Chemistry 17:149-163, or segments consisting of short-periodicity internal repeats, as determined by the XNU program of Claverie & States (1993) Computers and Chemistry 17:191-201, or, for BLASTN, by the DUST program of Tatusov and Lipman (unpublished, but available on the World Wide Web at ncbi.nlm.nih.gov [see http://www.ncbi.nlm.nih.gov]). Filtering can eliminate statistically significant but biologically uninteresting reports from the blast output (e.g., hits against common acidic-, basic- or proline-rich regions), leaving the more biologically interesting regions of the query sequence available for specific matching against database sequences.

In the Claims

8. (Twice Amended) A nucleic acid encoding a 5'OT-EST polypeptide [, wherein said polypeptide comprises a sequence] comprising an amino acid sequence selected from the group

consisting of (a) the sequences set forth in any one of SEQ ID Nos. 2, 4, or 6, and (b) sequences which are at least 90% homologous, as determined by BLAST analysis using default parameters, to the full length of said sequence[s] set forth in any one of SEQ ID Nos. 2, 4, or 6.

9. (Twice Amended) [A] The nucleic acid of [any one of claims 1-7] claim 8, having a sequence selected from the group consisting of [any one of] SEQ. ID. Nos. 1, 3, 5, 7, 16 or 17, [sequences] or a nucleic acid sequence which [are hybridisable under stringent conditions with an oligonucleotide comprising 20 contiguous based form any one of SEQ ID Nos. 1, 3, 5, 7, 16, or 17; sequences substantially] is at least 90% homologous to [any one of] the full length of SEQ ID Nos. 1, 3, 5, 7, 16, or 17 [and sequences complementary thereto] as determined by BLAST analysis using default parameters.

10. (Twice Amended) The nucleic acid of claim 9, comprising the sequence with SEQ ID NO: 31
[ATGTTGCGGGCTTTGAACCGCCTGGCCGCGCGGCCCGGGGGCCAGCCCCCAACCCT
GCTCCTTCTGCCCGTGCGCGGCCCACGGCCCCGCTCATTCTCGGCTCCTTTTTCCTCG
CAGGATAGC] or an equivalent sequence which encodes the same polypeptide having regard to the degeneracy of the nucleic acid code, or a sequence [substantially] at least 90% homologous thereto over the full length of SEQ ID NO: 31, as determined by BLAST analysis using default parameters.

16. (Twice Amended) A method for producing a 5'OT-EST polypeptide having a sequence selected from the group consisting of (a) the sequences set forth in any one of SEQ ID Nos. 2, 4, 6, or (b) sequences which are at least 90% homologous as determined by BLAST analysis using default parameters to the full length of said sequences set forth in any one of SEQ ID Nos. 2, 4, or 6, comprising transforming a cell with a vector of any one of claims 11 to 14 and culturing the

cell to produce the polypeptide.

28. (Twice Amended) A diagnostic reagent for the detection of mutations, polymorphisms or other changes in 5'OT-EST which may predispose an individual to obesity, comprising at least one detectably labeled nucleic acid probe of 150 nucleotides or less which is capable of hybridizing to [5'OT-EST or a sequence at least 90% homologous to 5'OT-EST] a sequence selected from the group consisting of (a) any one of SEQ ID NOs 1, 3 or 5, and (b) a sequence at least 90% identical to the full length of a said sequence as determined by BLAST analysis using default parameters.

31. (Amended) The nucleic acid of claim 8, wherein said 5'OT-EST polypeptide [is a mutant 5'OT-EST polypeptide which], in vivo, modulates the obesity of an animal which expresses said [mutant] 5'OT-EST polypeptide.

32. (Amended) The nucleic acid of claim [30] 31, wherein said [animal which expresses said mutant] 5'OT-EST polypeptide modulates the obesity of a transgenic animal which expresses said 5'-OT-EST polypeptide [is a transgenic animal comprising a transgene encoding said mutant 5'OT-EST polyepeptide].

33. (Amended) The nucleic acid of any one of claims 8, [29,] 30, or 31 wherein said 5'OT-EST polypeptide comprises the sequence [PRPRSFSAPFSQDS] of SEQ ID NO: 37.

34. (Amended) The nucleic acid of any one of claims 8, [29,] 30, or 31 wherein said 5'OT-EST polypeptide comprises the sequence [MLRALNRLAARPGGQPPTLLLLPVRGPRPRSFSAPFSSQDS] of SEQ ID NO: 8.

35 (New) A method for the detection of mutations, polymorphisms or other changes in 5'OT-EST which may predispose an individual to obesity, said method comprising hybridizing a nucleic acid sample from an individual to a detectably labeled probe that is capable of

hybridizing to a sequence selected from the group consisting of (a) any one of SEQ ID NOs 1, 3 or 5, and (b) a sequence at least 90% identical over the full length of one of SEQ ID NOs 1, 3 or 5, wherein a mutation, polymorphism or other change in 5'OT-EST sequence in said individual is detected.